ALEXANDRA GATZIOS

Pharmacist
VUB (IVTD) – PhD student since February 2021

PROFILE

25 years old

Pharmacist

Member of IVTD and IC-3Rs

EDUCATION

Vrije Universiteit Brussel
Pharmaceutical Sciences - Master of Science in Drug Development
2020 *Magna cum laude*

CONTACT

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PROJECT OUTLINE

Development and application of a human stem cell-based *in vitro* model for studying NASH-fibrosis
February 2021–2025: Starting phase of the project.

Metabolic-associated fatty liver disease (MAFLD) is one of the most prevalent chronic liver diseases worldwide. MAFLD encompasses multiple disease stadia, ranging from benign liver steatosis to non-alcoholic steatohepatitis (NASH), fibrosis, cirrhosis and cancer. NASH often associates with liver fibrosis and is hence the tipping point to the life-threatening stages of MAFLD. Yet, no drugs against it are approved. This is partly due to a lack of suitable preclinical models. Animal models are not predictive and relevant for the human situation. Therefore, the prime objective of this research is to develop an *in vitro* human stem cell-based model that allows the investigation of NASH-related liver fibrosis.
Our research group demonstrated that postnatal human skin-derived precursors differentiated to hepatic progenitor-like cells (hSKP-HPC) are valuable for investigating the hepatic-specific effects of potential anti-NASH compounds. Yet, hepatic stellate cells fulfill a key role in further disease progression. Therefore, the first objective is to develop a protocol to differentiate hSKP to quiescent hepatic stellate cell-like cells (hSKP-HSC), based on the human embryonic development of these cells. The possibility to use small-molecules instead of growth factors will also be investigated to obtain a chemically well-defined differentiation protocol. The human immortalized HSC cell line LX-2 will serve as a benchmark for the molecular assays and the most promising protocol will be selected. Subsequently, the possibility to activate hSKP-HSC by different NASH-relevant factors will be studied. Then, anti-NASH compounds tested in phase 2/3 clinical trials will be tested to diminish the activation of hSKP-HSC, rendering insight in their potential for future clinical development. Ultimately, a co-culture model consisting of hSKP-HPC and hSKP-HSC will be created, allowing investigation of anti-lipogenic, anti-inflammatory and anti–fibrotic properties of novel anti-NASH compounds.

RESEARCH OUTPUT

Poster presentation Global NASH Congress – online congress
Global Engage, April 28th-29th 2021
Differentiation of multipotent human skin-derived precursors towards hepatic stellate cell-like cells for modelling liver fibrosis in vitro.

Review article in progress
Etiology-based in vitro modelling of NASH-fibrosis: towards precision medicine in early drug development.

ACTIVITIES

- **Online training course:** Safety assessment of cosmetics in the EU (VUB, February 1st – March 17th 2021)
- **Online congress:** Global NASH Congress (Global Engage, April 28th – 29th 2021)
- **Webinar:** NASH in 2021: The multi-system disease (PanNASH, June 22nd 2021)
- **Online workshops:** Cell health in 2D and 3D culture, Cell metabolism, Protein interactions (Promega, June 8th, 15th, 22nd and 29th 2021)

VUB-Leerstoel Mireille Aerens